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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 01/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,857	LEWIS ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-33* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/30/04; 4/30/04;* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-33 are pending.

Specification

Claim 16 is objected to because of the following informalities: there is an apparent typographical error in line 5 of said claim in which the capital letter "L" is located at the end of the chemical name "HFA 227." The Examiner respectfully suggests removing the letter "--L--" and inserting the word "to" on line 5 of claim 16 between the chemical names, "HFA 227" and "HFA 134a," respectively. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 16, 17, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16 and 17 are confusing because possible limitations are contained within parentheses. For example, claims 16 and 17 contain "(<4.7 μm)." The use of parentheses is improper, because it is uncertain whether the item contained within parentheses is intended as another claim limitation or if it is intended solely as an example. Regarding, claims 16 and 17, the Examiner respectfully suggests that "<4.7 μm" is made a subscript to the term fine particle dose to avoid any ambiguity.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-21, 23-27, 29, and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by McNally et al. (U.S. Patent No. 5,653,961).

McNally discloses pharmaceutical **solution aerosol formulations of butixocort propionate** as the sole active drug agent and a propellant selected from the group consisting of **1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof** (abstract). The propellants 1,1,1,2-tetrafluoroethane and 1,1,1,12,3,3,3-heptafluoropropane are also known as HFA 134a and HFA 227, respectively. Butixocort propionate is an active material.

McNally discloses that the formulations generally comprise **butixocort propionate** in amounts from about 0.1 to about 0.9 percent by weight (col. 2, lines23-25) and that **cosolvent** (e.g. **ethanol**, **propylene glycol**, and dimethyl ether) may be used to aid drug dissolution (col. 2, lines 50-55). Both ethanol and propylene glycol are alcohols. Propylene glycol is also a glycol- a compound having two hydroxyl moieties (Solomons, T. W. G. *Organic Chemistry, 6th ed.* John Wiley & Sons, Inc.: New York, 1992, pp 398 and 402). McNally discloses ethanol as the preferred cosolvent, which may constitute from about 3 to about 30 wt. % of the formulation.

McNally discloses that the preferred propellants can be selected from HFA 134a, HFA 227, and **mixtures thereof in any proportion** (col. 3, lines 10-12).

McNally discloses that the formulation of his invention may contain suitable excipients, including water (0.005 wt. % to 1 wt.%) (col. 3, lines25-37). Water is also a solvent.

McNally discloses that aerosol canisters equipped with conventional valves preferably metered dose valves can be used to deliver formulations of his invention and that the preferred container is an **aluminum aerosol vial** (col. 4, lines 9-10). McNally also discloses aluminum aerosol containers **coated with an epoxy resin** (see Table 3). An aerosol canister equipped with metered dose valves reads on an inhaler.

McNally discloses formulations in Examples 1-2 having a **respirable fraction** (i.e. the percent by weight of particles having an aerodynamic particle size less than 4.7 microns) ranging from **45% to 69%**. The term "respirable fraction" reads on the term "fine particle dose" in claim 16.

McNally does not disclose the vapor pressure of propylene glycol. However, the Examiner contends that propylene glycol inherently meets stated limitation of a "low volatility component" and cosolvent having a vapor pressure less than 3 kPa, because glycols, especially propylene glycol, have been identified in the instant specification as examples of suitable low volatility components.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over McNally et al. (U.S. Patent No. 5,653,961).

The teachings of McNally have been set forth above.

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention aware of McNally's teachings that one could use a cosolvent system comprising ethanol and $\leq$ 20% propylene glycol, because these compounds are taught by McNally as suitable cosolvents used to aid the dissolution of medicaments in hydrofluoroalkane aerosol formulations. It is obvious to combine compounds with the same function, in this case, functioning as cosolvents. Because McNally identified ethanol as the preferred cosolvent it

would have been obvious to a skilled artisan that it is desirable to use more ethanol than propylene glycol. Although McNally does not identify propylene glycol as a low volatility component, this is nonetheless a property of propylene glycol. The properties of a compound or composition cannot be separated from the compound/composition. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Furthermore, optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Claims 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over McNally et al. (U.S. Patent No. 5,653,961) as applied to claim 22 above, and further in view of Byron et al (U.S. Patent No. 5,190,029).

The teachings of McNally have been set forth above.

McNally lacks the teaching of compositions wherein the active agent is a beta-2 agonist or an anticholinergic.

Byron teaches **aerosol formulations** for use in metered dose inhalers that include **1,1,1,2-tetrafluoroethane (HFA 134a)** alone and in combination with other compounds as well as various hydrocarbon blends (abstract).

Byron teaches that agents commonly delivered by the inhalation route include bronchodilators (**Beta-2 agonists and anticholinergics**), **corticosteroids**, and anti-allergics (col. 1, lines 23-27).

Byron teaches in claim 1 an inhaler containing an aerosol formulation comprising a **dissolved** or dispersed **drug** and HFA 134a. The term drug reads on the term "active material."

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of McNally and Byron, because both inventors teach aerosol formulations comprising HFA 134a and medicaments for use in inhalers. It would have been apparent to a skilled artisan that the active material in an aerosol formulation could be an anticholinergic, corticosteroid, or beta-2 agonist, because these drugs are commonly delivered via inhalation (i.e. the route of administration operative in the use of inhalers).

Claims 16-24 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. (WO 98/34595). U.S. Patent No. 6,461,591 is being used as the English language equivalent of WO 98/34595.

Keller teaches **pressure-liquefied propellant mixture for aerosols**, comprising a fluorinated alkane, in particular **1,1,1,2-tetrafluoroethane (HFA 134a)** and/or **1,1,1,2,3,3,3-heptafluoropropane (HFA 227)**, and carbon dioxide (abstract).

Keller teaches that his invention also relates to medicinal aerosol formulations and lists suitable hydrofluoroalkane propellants, including HFA 227, HFA 134a, and **mixtures thereof** (col. 7, lines 14-31).

Keller teaches that suitable pharmaceutically active compounds include **fundamentally all active compounds**, which can be administered, including **beta-mimetics** (e.g. formoterol), **corticosteroids** (e.g. beclomethasone, budesonide, and butixocort), **anticholinergics** (e.g. ipratropium bromide), etc. These active compounds can be used in the form of their isomers, enantiomers or racemates, and pharmaceutically acceptable salts. The optimum amount of the active compound in the formulations depends on the particular compound (col. 7, lines 48-67; col. 8, lines 1-67; and col. 9, lines 1-3).

Keller teaches that his invented aerosol formulations are suitable for solution formulations, and may also include cosolvents and surface-active agents –surfactants- (col. 9, lines 34-37). Examples of acceptable cosolvents include, water, **lower alcohols** (e.g. ethanol), **ethylene glycol, propylene glycol**, etc. Cosolvents are present in amounts of approximately **0.1 to 30% by weight,** wherein ethanol is preferred (col. 9, lines 46-60). Suitable surfactants include **oleic acid** and can be used in amounts ranging from **0.001 to 5% by weight** (col. 10, lines 10-22).

Keller teaches that the particle size distribution spectrum can be adjusted to that the active compound can be deposited in a targeted manner at the desired site in the lung (col. 10, lines 61-65).

Keller teaches that the aerosol formulations can be sealed into customary **pressure-tight containers with customary commercial metering valves and atomized using customary commercial mouth tube adapters** (col. 11, lines 11-15). Said containers taught by Keller read on inhalers used to dispense aerosols.

Keller teaches that the free particle dosage and associated mass median aerodynamic diameter (MMAD) in Example 1, Table 1, wherein the **MMAD is 1.3 microns**.

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention aware of Keller's teachings that one could use a cosolvent system comprising ethanol and ≤ 20% propylene glycol or ethylene glycol, because Keller teaches these compounds as suitable cosolvents. It is obvious to combine compounds with the same function, in this case, functioning as cosolvents. Because Keller identified ethanol as the preferred cosolvent it would have been obvious to a skilled artisan that it is desirable to use more ethanol than propylene glycol or ethylene glycol. Keller does not teach low volatility components or the vapor pressure associated with these low volatility components. Keller does not identify propylene glycol or ethylene glycol as low volatility components; however, this is nonetheless a property of these compounds, because they are identified in the instant specification as low volatility components. The properties of a compounds or compositions cannot be separated from the compounds/compositions. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Furthermore, optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Keller does not teach a range of respirable fractions of MMAD's, but does provide an example in which the his invented formulations had an MMAD of 1.3 microns. The MMAD of an aerosol is

a physical characteristic that a person of ordinary skill in the art would optimize to obtain a formulation with the desired properties. Therefore, it would have been obvious to a skilled artisan to optimize the MMAD and fine particle dose of Keller's formulations.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-33 (all claims) are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14, and 16-29 of U.S. Patent No. 6,713,047. Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Claims 16-24, 27, and 30-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 and 22-24 of U.S. Patent No. 6,964,759. Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers

Claims 16-18, 21-24, and 27-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-44 of copending application 09/831,888 (copending '888). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Specifically, the inhaler solution of copending '888 is obvious over the aerosol produced from a solution comprising the composition stated in claim 16 of the instant application.

Claims 16-24 and 30-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-20 and 29-31 of copending application 10/204,307 (copending '307). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Claims 16, 17, 24, 27, 29, 31, and 32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over all the claims of copending application 10/244,519 (copending '519). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Claims 16-18, 21, 29, and 33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 14, 17, 19 and 20 of copending application 10/275,891 (copending '891). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Claims 16, 17, 24, 29, and 31-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over all the claims of copending application 10/290,225 (copending '225). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions

comprising active materials and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Claims 16-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13, 18, and 21-23 of copending application 10/435,032 (copending '032). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Claims 16-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13, 18, and 21-23 of copending application 10/435,354 (copending '354). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers.

Other Matter

It is noted that the Applicant has provided continuity data on an Application Data sheet. The Examiner respectfully suggests that the Applicant also supply the continuity data at the first line of the specification.

Conclusion

Claim 16 is objected. All claims are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni (Paddy) Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James H. Alstrum-Acevedo, Ph.D.
Examiner

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER